Curriculum Vitae

Date: May 2009

Name	First Name	Marital Status	Nationality
Manley	Paul	Divorced	U.K.
Date of birth	**Mother Language**	**Other Languages**	
25.12.1953	English	German	
Home Address		**Novartis internal address**	
Bruggweg 12 CH-4144 Arlesheim Switzerland		WKL-136.4.86 CH-4002 Basel Switzerland	
Email		**Pers.-No**	
paul.manley@novartis.com		5002315	

Professional Experience
Summary:

28 Years medicinal chemistry research experience in pharmaceutical industry (21 in Sandoz - Novartis), with extensive experience as a Program / Project Team Leader / Global Project Team Representative (Glivec & Tasigna). A proven track record for drug discovery in the Oncology, Respiratory, Cardiovascular and Anti-infective disease areas.

Key contributions to Oncology DA: Leadership of Novartis-SGX research collaboration. Recognising need for Glivec follow-up in 2000, rapid initiation of Bcr-Abl Program and discovery of AMN107 (nilotinib; ESC 2002, PoC 2004, NDA 2006) and championing development of drug to launch of Tasigna® in 2007 and beyond; building Jak2 program; initiation of Flt3 Program with identification of PKC412 as clinical candidate; development compounds for Angiogenesis Program.

Key contributions to Respiratory DA: Leadership of PDE4D Program with development compounds; deputy leadership of K-Channel Activator Program with Clinical Phase I compound (KCO 912).

Organisation of Scientific Meetings: Kinase Inhibitor sessions at European Med Chem Symposium (2006) and Medicinal Chemistry Session at 229th ACS (2005).

Organisation of Novartis Workshops: "Angiogenesis"; "Target & Lead Selection"; "Pharmacophore Modelling and Virtual Screening".

Faculty Member: Chronic myeloid leukaemia workshops, 2005, 6 & 7; Swiss Med. Chem. School, 2002 & 4; Novartis Med. Chem. Workshop, 2004.
Regularly Chair scientific meetings and reviewer of medicinal chemistry and oncology drug scientific publications.

Professional Experience

Career History:

1998 to date: NIBR Oncology: Principal Research Investigator; Novartis Leading Scientist.

Program Team Head: Leader of NIBR/SGX research collaboration (since 2006). Joint Leader of NIBR/GNF Bcr-Abl Program (2000-2006). Leader of JAK2 Program 2004-2005. Leader of Flt3 Program 2001-2002.

Global Project Team Research Representative: Tasigna (since 8/2004); Glivec (since 10/20080.

Chemistry Laboratory Head (1998 to date).

Scientific Chemistry Expert: Oncology Department (1999-2001).

Additional Responsibilities: Compound Champion AKU557/AMN107, AAL993. MMP-Program liason between Basel (Research and Pride) and Japan. Compound Profiling Team Head for PDE472A (1998-99). Workshops organised: "Angiogenesis"; "Target & Lead Selection"; "Pharmacophore Modeling and Virtual Screening".

RDTA Development Support: PCO912; PDE472.

Achievements: Design and synthesis of Bcr-Abl inhibitors: CSP(2007) **BQM647**; CSP(2005) **BGG463**; CSP(2004) **BBT594/LBY977**; ESC(2002) **AKU557/AMN107**). VEGF kinase inhibitors: ESC(2002) **AAX433/ABP309/AEB342**; ESC(2000) **AAL993**.

Novartis Leading Scientist award: 2007

ONC BU Presidents Prize 2004, 2006 and 2007: **AMN107 / Tasigna**.

1989-98: Sandoz / Novartis Respiratory Diseases

Program Team Head: Phosphodiesterase Inhibitors.

Chemistry Laboratory Head.

Additional Responsibilities: Steering Committee collaboration (Columbia University, NY): Utility of PDE inhibitors.

Achievements: Design and synthesis of PDE 4 Inhibitors (**FSC 229-472**; **ICC 222-520**). FSC declaration of **PDE472A**. Synthesis of NVP-AAD997-NX1 (thus confirming structure of PCO912 metabolite, M16). Design and synthesis of K_{ATP}-Activators (Phase I compound **EDP KCO 912, ICC 217-744**).

1986-9: Sandoz Cardiovascular

Chemistry Laboratory Head.

Achievements: Design and synthesis of K_{ATP}-Activators (**PCI 999**; design & synthesis of radioligand, marketed by Amersham).

1979-86 Searle Research & Development, High Wycombe, Bucks. HP12 4HL:

Group Leader (1981-86): Platelet & Vascular Dysfunction.

Research Investigator (1979-81): Antiinfectives.

Achievements: Design and synthesis of TxA_2 Synthase Inhibitors (Clinical Development Candidates), PDE 3 inhibitors, PAF antagonists, thrombin antagonists, Zenoconazole (orally-active antifungal). **Searle Merit Award (1986):** 'Discovery of two series of Thromboxane Synthase Inhibitors and two series of PAF-receptor antagonists'.

Education

Queen Elisabeth's Hospital School (1964-71)

Leicester University / Glaxo (1971-76): Applied chemistry; B.Sc. (Hons).

Liverpool University (1976-79): Organic chemistry; Ph.D.

G.D. Searle: C. Chem.; MRSC.

Unit Med. Chem., Oncology Basel **Function** Global Project Team Representative; Programme Team Head; Lab. Head: Sr. Research Investigator 2.		**Superior** Marc Lang
Promotions/Awards KTC **Novartis Presidents Award (2004):** AMN107 Early Development Team **Novartis Pharma Team (President's) Award honorary mention (2005):** AMN107 Development **Novartis Pharma Team (President's) Award (2007):** Tasigna Development **Novartis Leading Scientist Award (2007)**		**Special Tasks** IPT Representative (2004-) Programme/Project Team Head Chemistry Expert (1999-2001) Compound Champion Compound Profiling Team Head

Internal/External Courses/Sabbaticals

Courses:
As faculty: Novartis GDC Med. Chem. Workshop; Swiss Med. Chem. Course (2004; 2002); Nordwijkerhout Med Chem course (2005); Global Opinion Leader Summit CML 2006.
As delegate: Vision to Practice, Risk Management, Negotiation Skills, Leading Teams

Sabbaticals:
None

Publications

1. Paul W. Manley, Peter Drueckes, Gabriele Fendrich, Pascal Furet, Janis Liebetanz, Georg Martiny-Baron, Jürgen Mestan, Jörg Trappe, Markus Wartmann, Doriano Fabbro Extended kinase rofile and properties of the protein kinase inhibitor Nilotinib. *Biochim. Biphys. Acta* **2009**, *in press*.

2. P.W. Manley, S. Cowan-Jacob, D. Fabbro, G. Fendrich, W. Jahnke, J. Liebetanz, J. Mestan, A. Strauss, N. Vajpai, S. Grzesiek. Differences in the kinase binding modes of imatinib, nilotinib and dasatinib are reflected in Abl transphosphorylation assays. Acta Biochimica Polonica 2009;56:S4.

3. D. Fabbro, M. Warmuth, F.J. Adrian, P.W. Manley, S.W. Cowan-Jacob, G. Fendrich, A. Strauss, W. Jahnke, J. Liebetanz, J. Mestan, N. Vajpai, S. Grzesiek, J. Zhang, N. Gray. Acta Biochimica Polonica 2009;56:S5.

4. Eck, Michael J.; Manley, Paul W. The interplay of structural information and functional studies in kinase drug design: insights from BCR-Abl. Current Opin. Cell Biol. 2009:21:288-295.

5. Mahon F-X, Hayette S, Lagarde V, Belloc F, Turcq B, Nicolini F, Belanger C, Manley PW, Leroy C, Etienne G, Roche S, and Pasquet J-M. Evidence that Resistance to Nilotinib May Be Due to BCR-ABL, Pgp, or Src Kinase Overexpression. Cancer Res 2008;68:9809–16.

6. Cross, N. C. P.; Daley, G. Q.; Green, A. R.; Hughes, T. P.; Jamieson, C.; Manley, P.; Mughal, T.; Perrotti, D.; Radich, J.; Skoda, R.; Soverini, S.; Vainchenker, W.; Verstovsek, S.; Villeval, J.-L.; Goldman, J. M. BCR-ABL1-positive CML and BCR-ABL1-negative chronic myeloproliferative disorders: some common and contrasting features. Leukemia 2008;22:1975-1989.

7. Day E, Waters B, Spiegel K, Alnadaf T, Manley PW, Buchdunger E, Walker C, Jarai G. Inhibition of collagen induced discoidin domain receptor 1 and 2 activation by imatinib, nilotinib and dasatinib. Eur J Pharmacol 2008;599:44-53.

8. Dierks C, Beigi R, Guo G-R, Zirlik K, Stegert MR, Manley PW, Trussell C, Schmitt-Graeff A, Landwerlin K, Veelken H, Warmuth M. Expansion of Bcr-Abl-Positive Leukemic Stem Cells Is Dependent on Hedgehog Pathway Activation. Cancer Cell 2008;14:238.

9. Ganapathipillai, S.S.; Medova, M.; Aebersold, D.M.; Manley, P.W.; Berthou, S.; Streit, B.; Blank-Liss, W.; Greiner, R.H.; Rothen-Rutishauser, B.; Zimmer, Y. Coupling of Mutated Met Variants to DNA Repair via Abl and Rad51. Cancer Research 2008;68:5769-5777.

10. VajpaiN., Strauss A., Fendrich G., Cowan-Jacob S.W., Manley P.W., Grzesiek S., Jahnke W. Solution conformations and dynamics of ABL kinase inhibitor complexes determined by NMR substantiate the different binding modes of imatinib/nilotinib and dasatinib. J. Biol. Chem., 2008; 283:18292-18302.

11. Vajpai N., Strauss A., Fendrich G., Cowan-Jacob S.W., Manley P.W., Grzesiek S., Jahnke W. Backbone NMR resonance assignment of the Abelson kinase domain in complex with Imatinib. *Biomolecular NMR* Assign 2008;2:41-42.

12. Konig H, Holtz M, Modi H, Manley P, Holyoake T.L., Forman S.J., and Bhatia R. Enhanced BCR-ABL kinase inhibition does not result in increased inhibition of downstream signaling pathways or increased growth suppression in CML progenitors.

Leukemia 2008;22:748-755.

13. Gleixner KV, Mayerhofer M, Sonneck K, Gruze A, Samorapoompichit P, Baumgartner C, Lee FY, Aichberger KJ, Manley PW, Fabbro D, Pickl WF, Sillaber C, Valent P. Synergistic growth-inhibitory effects of two tyrosine kinase inhibitors, dasatinib and PKC412, on neoplastic mast cells expressing the D816V-mutated oncogenic variant of KIT. Haematologica 2007;92:1451-1459.

14. White DL, Saunders VA, Dang P, Engler J, Venables A, Zrim S, Zannettino A, Lynch K, Manley PW, and Hughes T. Most CML patients who have a suboptimal response to imatinib have low OCT-1 activity: higher doses of imatinib may overcome the negative impact of low OCT-1 activity. Blood 2007;110:4064-4072.

15. Shemon AN, Sluyter R, Stokes L, Manley PW, Wiley JS. Inhibition of the human P2X7 receptor by a novel protein tyrosine kinase antagonist. Biochemical and Biophysical Research Communications 2008;365:515-520.

16. Brownlow N, Russell AE, Saravanapavan H, Wiesmann M, Murray JM, Manley PW and Dibb NJ. Comparison of nilotinib and imatinib inhibition of FMS receptor signaling, macrophage production and osteoclastogenesis. Leukemia 2008;22:649-652.

17. White DL, Saunders VA, Dang P, Engler J, Venables A, Zrim S, Zannettino A, Lynch K, Manley PW, and Hughes T. Most CML patients who have a suboptimal response to imatinib have low OCT-1 Activity. Higher doses of imatinib may overcome the negative impact of low OCT-1 Activity. Blood First Edition Paper, prepublished online August 30, 2007;

18. Weisberg E, Manley PW, Cowan-Jacob SW, Hochhaus A, Griffin JD. Second generation inhibitors of BCR-ABL for the treatment of imatinib-resistant CML. Nature Rev. Cancer 2007;7:345-356.

19. White DL, Saunders VA, Lynch K, Manley PW, and Hughes TP. Imatinib increases the intracellular concentration of nilotinib which may explain the observed synergy between these drugs. Blood 2007;109:3609-3610.

20. Ray A, Cowan-Jacob SW, Manley PW, Mestan J, and Griffin JD. Identification of Bcr/Abl point mutations conferring resistance to the Abl kinase inhibitor AMN107 (Nilotinib) by a random mutagenesis study. Blood 2007;109:5011-5015.

21. Wang Y, Cai D, Brendel C, Barrett C, Erben P, Manley PW, Hochhaus A, Neubauer A, and Burchert A. Adaptive secretion of the granulocyte macrophage colony stimulating factor (GM-CSF) mediates imatinib- and nilotinib-resistance in BCR/ABL-positive progenitors via Jak-2/STAT-5 pathway activation. Blood 2007;109:2147-2155.

22. Cowan-Jacob, S.W.; Fendrich, G.; Floersheimer, A.; Furet, P.; Liebetanz, J.; Rummel, G.; Rheinberger, P.; Centeleghe, M.; Fabbro, D.; Manley, P.W. Structural biology contributions to the discovery of drugs to treat chronic myelogenous leukaemia. Acta Crystallographica. Section D: Biological Crystallography 2007;D63:80-93.

23. Manley PW, Cowan-Jacob SW, Fendrich G, Strauss A, Vapai N, Grzesiek S, Jahnke W. Bcr-Abl Binding Modes of Dasatinib, Imatinib and Nilotinib: An NMR Study. Blood 2006;108:224a.

24. Weisberg E, Catley L, Wright R, Andrew Kung1, Moreno D, Banerji L, Ray A, Manley PW, Mestan J, Fabbro D, Jiang J, Hall-Meyers E, Callahan L, Dellagatta JL, Kung A and Griffin JD. Beneficial Effects of Combining Nilotinib and Imatinib in Pre-Clinical Models of BCR/ABL+ Leukemias. Blood 2007;109:2112-2120.

25. Weisberg E, Wright R, Jiang J, Ray A, Moreno D, Manley P, Fabbro D, Hall-Meyers E,

Catley L, Podar K, Kung AL, Griffin JD. Effects of PKC412, nilotinib and imatinib against GIST-associated PDGFRA mutants conferring differential sensitivity to imatinib. Gastroenterology 2006; 131:1734-1742.

26. Verstovsek S, Akin C, Manshouri T, Quintás-Cardama A, Huynh L, Manley P, Tefferi A, Cortes J, Giles FJ, Kantarjian H. Effects of AMN107, a novel aminopyrimidine tyrosine kinase inhibitor, on human mast cells bearing wild-type or mutated codon 816 c-kit. Leukemia Res. 2006;30:1365-1370.

27. Verstovsek S, Giles FJ, Quintás-Cardama A, Manshouri T, Huynh L, Manley P, Cortes J, Tefferi A, Kantarjian H. Activity of AMN107, a novel aminopyrimidine tyrosine kinase inhibitor, against human FIP1L1-PDGFR-α-expressing cells. Leukemia Res. 2006;30:1499-1505.

28. Weisberg E, Manley P, Mestan J, Cowan-Jacob S, Ray A, Griffin JD. AMN107 (nilotinib): a novel and selective inhibitor of BCR-ABL. Br. J. Cancer 2006;94:1765-1769.

29. von Bubnoff N, Manley PW, Mestan J, Sanger J, Peschel C, Duyster J. Bcr-Abl resistance screening predicts a limited spectrum of point mutations to be associated with clinical resistance to the Abl kinase inhibitor nilotinib (AMN107). Blood 2006, 108, 1328-1333.

30. White DL, Saunders VA, Dang P, Engler J, Zannettino AC, Cambareri AC, Quinn SR, Manley PW, Hughes TP. OCT-1 mediated influx is a key determinant of the intracellular uptake of imatinib but not nilotinib (AMN107): reduced OCT-1 activity is the cause of low in vitro sensitivity to imatinib. Blood, 2006, 108:697-704.

31. Kantarjian H, Giles F, Wunderle L, Bhalla K, O'Brien S, Wassmann B, Tanaka C, Manley P, Rae P, Mietlowski W, Bochinski K, Hochhaus A, Griffin JD, Hoelzer D, Albitar M, Dugan M, Cortes J, Alland L, Ottmann OG. AMN107, a Novel, Highly Active, Selective Bcr-Abl Tyrosine Kinase Inhibitor in Patients with Philadelphia Chromosome (Ph) positive Chronic Myelogenous Leukemia (CML) or Acute Lymphocytic Leukemia (ALL) who are Resistant to Imatinib Mesylate Therapy. New Engl J Med 2006, 354, 2542-2551.

32. Fiskus W, Pranpat M, Bali P, Balasis M, Kumaraswamy S, Boyapalle S, Rocha K, Wu J, Giles F, Manley PW, Atadja P, and Bhalla K. Combined Effects of Novel Tyrosine Kinase Inhibitor AMN107 and Histone Deacetylase Inhibitor LBH589 against Bcr-Abl Expressing Human Leukemia Cells. Blood, 2006, 108:645-52.

33. Prenen H, Guetens G, de Boeck G, Debiec-Rychter M, Manley P, Schöffski P, van Oosterom AT, de Bruijn E. Cellular Uptake of the Tyrosine Kinase Inhibitors Imatinib and AMN107 in Gastrointestinal Stromal Tumor Cell Lines. Pharmacology 2006;77:11-16.

34. Adrian FJ, Ding Q, Sim T, Valenta A, Sloan S, Liu Y, Zhang G, Hur W, Ding S, Manley P, Mestan D, Fabbro D, Gray N. Allosteric inhibitors of Bcr-Abl dependent proliferation. Nature Chem. Biol. 2006;2:95-102.

35. P.W. Manley, S.W. Cowan-Jacob, J. Mestan. Advances in the Structural Biology, Design and Clinical Development of Bcr-Abl Kinase Inhibitors for the Treatment of Chronic Myeloid Leukaemia. *Biochim. Biphys. Acta* **2005**, 1754, 3-13.

36. P.W. Manley, S.W. Cowan-Jacob, G. Fendrich, J. Mestan. Molecular Interactions Between the Highly Selective pan-Bcr-Abl Inhibitor, AMN107, and the Tyrosine Kinase Domain of Abl. *Blood* **2005**, 106, 940a-941a.

37. Fabbro, D., Fendrich, G., Guez, V., Meyer, T., Furet, P., Mestan, J., Griffin, J. D., Manley, P. W., & Cowan-Jacob, S. W. "Targeted therapy with imatinib: An exception or a

rule?", Handbook of Experimental Pharmacology (2005), vol.167, Inhibitors of Protein Kinases and Protein Phosphates, pp. 361-389.

38. K.V. Gleixner, M. Mayerhofer, K.J. Aichberger, S. Derdak, K. Sonneck, A. Böhm, A. Gruze, P. Samorapoompichit, P.W. Manley, D. Fabbro, W.F. Pickl, C. Sillaber, P. Valent. PKC412 inhibits in vitro growth of neoplastic human mast cells expressing the D816V-mutated variant of KIT: comparison with AMN107, imatinib, and cladribine (2CdA), and evaluation of cooperative drug effects. *Blood* **2006**, 107, 752-759.
39. E.H. Stover, J. Chen, B.H. Lee, J. Cools, E. McDowell, J. Adelsperger, D. Cullen, A. Coburn, S.A. Moore, R. Okabe, D. Fabbro, P.W. Manley, J.D. Griffin, D.G. Gilliland, The small molecule tyrosine kinase inhibitor AMN107 inhibits TEL-PDGFRβ and FIP1L1-PDGFRα in vitro and in vivo, *Blood* **2005**, 106, 3206-3213.
40. Golemovic M, Verstovsek S, Francis Giles F, Cortes J, Manshouri T, Manley PW, Mestan J, Dugan M, Alland L, Griffin JD, Kantarjian H, Beran M. AMN107, a novel aminopyrimidine inhibitor of Bcr-Abl, has in vitro activity against imatinib-resistant chronic myeloid leukemia. *Clinical Cancer Research*, **2005**, 11, 4941-4947.
41. Verstovsek S., Golemovic M., Kantarjian H., Manshouri T., Estrov Z., Manley P., Sun T., Arlinghaus R, Alland L., Dugan M., Cortes J., Giles F., Beran M. AMN107, a Novel Aminopyrimidine Inhibitor of p190 Bcr-Abl Activation and of In Vitro Proliferation of Philadelphia–Positive Acute Lymphoblastic Leukemia Cells. *Cancer* **2005**, 104, 1230-1236.
42. S.W. Cowan-Jacob, G. Fendrich, P.W. Manley, W. Jahnke, D. Fabbro, J. Liebetanz, T. Meyer, The Crystal Structure of a c-Src Complex in an Active Conformation Suggests Possible Steps in c-Src Activation, *Structure* **2005**, 13, 861-871.
43. P.W. Manley, S. Cowan-Jacob, J. Mestan, Advances in the Structural Biology, Design and Clinical Development of Bcr-Abl Kinase Inhibitors for the Treatment of Chronic Myelogenous Leukemia. *Cell. Mol. Biol. Lett.* **2005**, 10, 62S-65S.
44. T.J. Boggon, Y. Li, P. Manley, M.J. Eck. Crystal structure of the Jak3 kinase domain in complex with staurosporine analogue AFN941. *Blood* **2005**, 106, 996-1002.
45. T. O'Hare, D.K. Walters, E.P. Stoffregen, T. Jia, P.W. Manley, J. Mestan, S. Cowan-Jacob, M.C. Heinrich, M.W.N. Deininger, B.J. Druker. In vitro activity of Bcr-Abl inhibitors AMN107 and BMS-354825 against clinically relevant imatinib-resistant Abl kinase domain mutants. *Cancer Res.* **2005**, 65, 4500-4505.
46. Bold, G.; Bruggen, J.; Furet, P.; Manley, P. W.; Mestan, J.; Schnell, C; Stark, W.; Wood, J. M. Anthranilic Acid Derivatives: VEGF-R Kinase Inhibitors for Anti-angiogenic Therapy in Cancer. *Drugs of the Future* **2004**, 29A, 33.
47. E. Weisberg, P.W. Manley, W. Breitenstein, Josef Brüggen, S.W. Cowan-Jacob, A. Ray, B. Huntly, D Fabbro, G. Fendrich, E. Hall-Meyers, A.L. Kung, Jürgen Mestan, G.Q. Daley, L. Callahan, L. Catley, C. Cavazza, M. Azam, D. Neuberg, R.D. Wright, D.G. Gilliland and J.D. Griffin. AMN107: Characterization of a novel inhibitor of both wild-type and imatinib-resistant mutant Bcr-Abl in vitro and in murine models of leukemia. *Cancer Cell*, **2005**, 7, 129-141.
48. B. Cutting, A. Strauss, G. Fendrich, P.W. Manley, W. Jahnke. NMR resonance assignment of selectively labeled proteins by the use of paramagnetic ligands. *J. Biomol. NMR*, **2004**, *30*, 205-210.
49. J. Mestan, E. Weisberg, S. Cowan-Jacob, D. Fabbro, P. Furet, G. Fendrich, G. Goutte, D. Kempf, M. Gaugler, J. D. Griffin, P. W. Manley. AMN107: In vitro profile of a new inhibitor of the tyrosine kinase activity of Bcr-Abl. *Blood*, **2004**, *102* (Suppl.), 546a. #1978.
50. J.D. Griffin, D. Fabbro, G. Fendrich, B. Huntly, S. Cowan-Jacob, A. Kung, J. Mestan, E. Weisberg, G. Gilliland, P.W. Manley. AMN107: Efficacy as a selective inhibitor of the tyrosine kinase activity of Bcr-Abl in murine leukemia models. *Blood*, **2004**, *102*

(Suppl.), 160a. #551.
51. G. Bold, J. Brüggen, P. Furet, P.W. Manley, J. Mestan, C.R. Schnell, W. Stark, J. Wood. Anthranilic Acid Derivatives: VEGF-R Kinase Inhibitors for Anti-angiogenic Therapy in Cancer. Drugs of the Future **2004**, *29A*, 33.
52. P.W. Manley, W. Breitenstein, J. Brüggen, S. W. Cowan-Jacob, P. Furet, J. Mestan, T. Meyer. Urea-derivatives of STI571 as inhibitors of Bcr-Abl and PDGFR kinases. *Bioorg. Med. Chem. Lett.*, **2004**, *14*, 5793-5797.
53. P.W. Manley, G. Bold, J. Brüggen, G. Fendrich, P. Furet, J. Mestan, C. Schnell, B. Stolz, T. Meyer, B. Meyhack, W. Stark, A. Strauss, J. Wood. Advances in the Structural Biology, Design and Clinical Development of VEGF-R Kinase Inhibitors for the Treatment of Angiogenesis. Biochim. Biophys. Acta **2004**, *1697*, 17-27.
54. S.W. Cowan-Jacob, V. Guez, J.D. Griffin, D. Fabbro, G. Fendrich, P. Furet, J. Liebetanz, J. Mestan, P.W. Manley. Bcr-Abl Kinase Mutations and Drug Resistance to Imatinib (STI571) in Chronic Myelogenous Leukemia. *Mini Rev. Med. Chem.* **2004**, *4*, 285-299.
55. J. Mestan, D. Kempf, G. Goutte, J. A. Fletcher, P. W. Manley. A New ELISA for Cellular c-Kit Phosphorylation: Activity of STI571 Compared to That of Other Protein Kinase Inhibitors. *Blood*, **2003**, *101* (Suppl.), ??a. abstr 4387.
56. P. W. Manley, G. Bold, J. Brüggen, G. Fendrich, P. Furet, J. Mestan, T. Meyer, B. Meyhack, C. Schnell, W. Stark, A Strauss, J. Wood. 2-[(4-Pyridinylmethyl)amino]-*N*-[3-(trifluoromethyl)-phenyl]-benzamide: A novel, antiangiogenic VEGF receptor kinase inhibitor. *Chimia* **2003**, *57*, 396.
57. Brian Cutting , André Strauss, Gabriele Fendrich, Paul W. Manley, Wolfgang Jahnke. Biomolecular NMR Tools to Accelerate Investigations of Protein-Ligand Complexes : Towards an NMR Understanding of the cAbl-Glivec Mode of Binding. *Chimia* **2003**, *57*, 396.
58. Pascal Furet, Guido Bold, Francesco Hofmann, Paul Manley, Thomas Meyer and Karl-Heinz Altmann. Identification of a new chemical class of potent angiogenesis inhibitors based on conformational considerations and database searching. *Bioorg. Med. Chem. Lett.*, **2003**, *13*, 2967-2971.
59. Jan Cools, Elizabeth H. Stover, Christina L. Boulton, Jason Gotlib, Robert D. Legare, Sonia M. Amaral, Nicole Duclos, Rebecca Rowan, David P. Curley, Jeffrey L. Kutok, Benjamin H. Lee, Ifor R. Williams, Steven E. Coutre, Richard M. Stone, Daniel J. DeAngelo, Peter Marynen PhD, Paul Manley, Thomas Meyer, Doriano Fabbro, Donna Neuberg, Ellen Weisberg, James D. Griffin, and D. Gary Gilliland PKC412 overcomes resistance to imatinib in a murine model of FIP1L1-PDGFRα-induced myeloproliferative disease. *Cancer Cell*, **2003**, 459-469.
60. P. W. Manley, G. Bold, G. Fendrich, P. Furet, J. Mestan, T. Meyer, B. Meyhack, W. Stark, A. Strauss, J. Wood. Advances with VEGF-R Kinase Inhibitors for the Treatment of Angiogenesis. *Cell Mol. Biol. Lett.* **2003**, *8(2A)*, 532-3.
61. P.W. Manley, M. Acemoglu, W. Marterer and W. Pachinger. Large scale Nigishi coupling as applied to the synthesis of PDE472, an inhibitor of phosphodiesterase type 4D. *Org. Proc. Res. Dev.* **2003**, *7*, 436-445.
62. Markus Warmuth, Nicola Simon, Olga Mitina, Ruth Mathes, Doriano Fabbro, Paul W Manley, Elisabeth Buchdunger, Karin Forster, Ismail Moarefi, and Michael Hallek. Dual-specific Src and Abl kinase inhibitors, PP1 and CGP76030, inhibit growth and survival of cells expressing STI571 resistant Bcr/Abl kinases. *Blood* **2003**, *101*, 664-672.
63. PW Manley, P Furet, G Bold, J Brüggen, J Mestan, T Meyer, CR Schnell, J Wood, M Haberey, A Huth, M Krüger, A Menrad, E Ottow, D Seidelmann, G Siemeister and KH Thierauch. Anthranilic Acid Amides: A novel class of antiangiogenic VEGF receptor kinase inhibitors. *J. Med. Chem.* **2002**, *45*, 5687-5693.
64. Cowan-Jacob SW, Fendrich G, Guez V, Liebetanz J, Fabbro D, Manley P. STI571

(IMATINIB): structural and enzymatic studies of interactions with Abl kinase and resistance mutants. *Acta Cryst.* **2002**, *A58(Suppl.)*, C289.
65. P.W. Manley, S.W. Cowan-Jacob, E. Buchdunger, D. Fabbro, G. Fendrich, P. Furet, T. Meyer, J. Zimmermann. Imatinib: a selective tyrosine kinase inhibitor. Eur. J. Cancer **2002**, 38, S19-S27.
66. Paul W. Manley, Georg Martiny-Baron, Jean-Marc Schlaeppi, Jeanette M. Wood.Anti-VEGF Therapy. *Expert Opinion on Biological Therapy* **2002**, *11*, 1715-1736.
67. Fabbro, Doriano; Ruetz, Stephan; Buchdunger, Elisabeth; Cowan-Jacob, Sandra W.; Fendrich, Gabriele; Liebetanz, Janis; Mestan, Jurgen; O'Reilly, Terence; Traxler, Peter; Chaudhuri, Bhabatosh; Fretz, Heinz; Zimmermann, Jurg; Meyer, Thomas; Caravatti, Giorgio; Furet, Pascal; Manley, Paul W. Protein kinases as targets for anticancer agents: from inhibitors to useful drugs. *Pharmacology & Therapeutics* **2002**, 93, 79-98.
68. Bold, Guido; Frei, Jorg; Furet, Pascal; Manley, Paul W.; Bruggen, Josef; Cozens, Robert; Ferrari, Stefano; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Jurgen; Meyer, Thomas; Wood, Jeanette M. CGP 79787D (PTK787/ZK222584), CGP 84738, NVP-AAC789, NVP-AAD777 and related 1-anilino-(4-pyridylmethyl)phthalazines as inhibitors of VEGF- and bFGF-induced angiogenesis. *Drugs of the Future* **2002**, 27, 43-55.
69. Ellen Weisberg, Christina Boulton, Louise M. Kelly, Paul Manley, Doriano Fabbro, Thomas Meyer, D. Gary Gilliland, James D. Griffin. Inhibition Of Mutant Flt3 Receptors In Leukemia Cells By The Small Molecule Tyrosine Kinase Inhibitor, PKC412. Cancer Cell **2002**, 1, 433-443.
70. Karl-Heinz Buchheit, Paul W. Manley, Ulrich Quast and John R. Fozard. KCO912: A potent and selective opener of ATP-dependent potassium (KATP) channels with selectivity for the airways. *N.S. Arch. Pharmacol.* **2002**, 365, 220-230.
71. Tyrosine kinase inhibitors: From rational design to clinical trials. Traxler P; Bold G; Buchdunger E; Caravatti G; Furet P; Manley P; O'Reilly T; Wood J; Zimmermann J. Medicinal Res. Rev. **2001**, *21*, 499-512.
72. Synthesis and characterization of a novel tritiated K_{ATP} channel opener with a benzopyran structure. Paul W. Manley, Cornelia Löffler-Walz, Ulrich Russ, Annette Hambrock, Thomas Moenius, Ulrich Quast. *Br. J. Pharmacol.* **2001**, *133*, 275.
73. Structure-activity studies supporting a postulated binding mode of STI571 to Abl kinase. Manley, Paul W.; Furet, Pascal; Buchdunger, Elisabeth; Fabbro, Doriano; Loiseleur, Olivier; Meyer, Thomas; Zimmermann, Juerg. *Abstr. Pap. - Am. Chem. Soc.* **2001**, 221st MEDI-143.
74. SU6668. Doriano Fabbro and Paul W. Manley. *Current Opinion in Investigational Drugs* **2001**, *2*, 1142.
75. Prospects for Anti-Angiogenic Therapies based upon VEGF Inhibition. Manley P, Furet P. *In Anticancer Agents: Frontiers in Cancer Chemotherapy*; Ojima I, Vite G, Altmann K, Eds.; ACS Symposium Series 796; American Chemical Society: Washington, DC, 2001; pp 282-298.
76. Potassium channel openers: Agents for the treatment of airway hyperreactivity. Fozard, John R.; Manley, Paul W. Prog. Respir. Res. **2001**, 31 (New Drugs for Asthma, Allergy and COPD), 77-80.
77. Case Study: Gleevec – A new Treatment Modality for CML. J. Zimmermann, E. Buchdunger, P. Manley. *Chimia* **2001**, 55, 598.
78. New Anilinophthalazines as Potent and Orally Well Absorbed Inhibitors of the VEGF Receptor Tyrosine Kinases Useful as Antagonists of Tumor-Driven Angiogenesis. Bold, G.; Altmann, K.-H.; Frei, J.; Lang, M.; Manley, P.W.; Traxler, P.; Wietfeld, B.; Buchdunger, E.; Cozens, R.; Ferrari, S.; Furet, P.; Hofmann, F.; Martiny-Baron, G.; Mestan, J.; Rösel, J.; Sills, M.; Stover, D.; Acemoglu, F.; Boss, E.; Emmenegger, R.; Lässer, L.; Masso, E.; Roth, R.; Schlachter, C.; Vetterli, W.; Wyss, D.; Wood, J.M. *J.*

Med. Chem. **2000**, *43*, 2310.
79. Atypical effect of minoxidil sulfate on guinea pig airways. Buchheit, K.H.; Hofmann, A.; Manley, P.; Pfannkuche, H.J.; Quast, U. *N.S. Arch. Pharmacol.* **2000**, *361*, 418-424.
80. Potassium channel activators for the treatment of asthma: 6-Pyridyl benzopyran derivatives. Manley, Paul W.; Buchheit, Karl-Heinz; Quast, Ulrich. Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), MEDI-274. Publisher: American Chemical Society, Washington, D. C. CODEN: 64RNAO. AN 1997:490031.
81. Atypical Effect of Minoxidil Sulphate on Guinea Pig Airways. Buchheit, K.H.; Hofmann, H.; Manley, P.; Pfannkuche, H.J.; Quast, U. *N.-S. Arch. Pharmacol.* 1997, *355*, R75.
82. PDE 4 Inhibitors: Design, synthesis and antiinflammatory activity of 4-(3-cyclopentylidenemethyl-4-methoxyphenyl)pyridine. Manley, P.W.; Bray, K.; Floersheim, P.; L.Mazzoni, L.; Müller, T. *Chimia*, 1996, *50*, 312.
83. Synthesis of and Radioligand Binding Studies with a Tritiated Pinacidil Analogue: Receptor Interactions of Structurally Different Classes of Potassium Channel Openers and Blockers. Manley, P.W.; Quast, U.; Andres, H; Bray, K. *J. Med. Chem.* 1993, *36*, 2004-2010.
84. Binding of the Potassium Channel Opener [^{3}H]-P1075 in Rat Isolated Aorta: Relationship to Functional Effects of Openers and Blockers. Quast, U.; Bray, K.; Andres, H.; Manley, P.W.; Baumlin, Y.; Dosogne, J. *Mol. Pharmacol.* 1993, *43*, 474-481.
85. 5-[6-1-(Cyclohexyl-1*H*-tetrazol-5-yl)hexyl]-1,8-naphthyridin-2-(1*H*)-one, SC-44368, a Potent Anti-Aggregatory Agent which Selectively Inhibits platelet Cyclic AMP Phosphodiesterase. Booth, R.F.G.; Manley, P.W.; Buckham, S.P.; Hassall. D.G.; Honey, A.C.; Lad, N.; Lunt, D.O.; Oswald, S.; Porter, R.A.; Tuffin, D.P. *Platelets.* 1992, *3*, 129-136.
86. Identification of a Specific Binding Site for Potassium Channel Openers in Rat Aorta. Quast, U.; Bray, K.; Baumlin, Y.; Andres, H.; Manley, P.W. *Jpn. J. Pharmacol.* 1992, *58*, 226P-231P.
87. Structure-Activity Studies of Potassium Channel Opening in Pinacidil-Type Cyanoguanidines, Nitroethenediamines, Thioureas and Ureas. Manley, P.W.; Quast, U. *J. Med. Chem.* 1992, *35*, 2327-2340.
88. Structure-Activity Studies of Potassium Channel Opening in Pinacidil-Type Cyanoguanidines and Nitroethenediamines. Manley, P.W.; Quast, U. *Chimia* 1991, *45*, 88-89.
89. Thrombin Receptor Antagonists. Ruda, E.M.; Scrutton, M.C.; Manley, P.W.; Tuffin, D.P. *Biochem. Pharmacol.* 1990, *39*, 373-381.
90. Identification of Small Peptide Analogues having Agonist and Antagonist Activity at the Platelet Thrombin Receptor. Ruda, E.M.; Petty, A.; Scrutton, M.C.; Tuffin, D.P.; Manley, P.W. *Biochem. Pharmacol.* 19988, *37*, 2417-2426.
91. Effect of SC38249, a Novel Substituted Imidazole, on Platelet Aggregation In Vitro and In Vivo. Lad, N.; Honey, A.C.; Lunt, D.O.; Booth, R.F.G.; Westwick, J.; Manley, P.W.; Tuffin, D.P. *Thromb. Haem.* 1988, *59*, 164-170.
92. Dibenzoquinazoline Diones as Antihypertensive Cyclic Guanosine Monophosphate Phosphodiesterase Inhibitors. Booth, R.F.G.; Buckham, S.P.; Lunt, D.O.; Manley, P.W.; Porter, R.A. *Biochem. Pharmacol.* 1987, *36*, 3517-3521.
93. Thromboxane Synthase Inhibitors. Synthesis and Pharmacological Activity of (*R*)-, (*S*)-, and (+/-)-2,2-Dimethyl-6-(2-(1*H*-imidazol-1-yl)-1-(((4-methoxyphenyl)-methoxy)methyl)ethoxy)hexanoic acids. Manley, P.W.; Tuffin, D.P.; Allanson, N.M.; Buckle, P.E.; Lad, N.; Lai, S.M.F.; Lunt, D.O.; Porter, R.A.; Wade, P.J. *J. Med. Chem.* 1987, *30*, 1812-1818.
94. Structure-Activity Relationships in an Imidazole-Based Series of Thromboxane Synthase

Inhibitors. Manley, P.W.; Allanson, N.M.; Booth, R.F.G.; Buckle, P.E.; Kuzniar, E.J.; Lad, N.; Lai, S.M.F.; Lunt, D.O.; Tuffin, D.P. *J. Med. Chem.* 1987, *30*, 1588-1595.
95. *N*-Azirin-3-yl and *N*-Indol-3-yl Azaxylylenes. Fishwick, C.W.G.; Randles, K.R.; Storr, R.C.; Manley, P.W. *Tet. Lett.* 1985, *26*, 3053-3056.
96. A Simple Route to *C*-Functionalised Azaxylylenes and Diazaxylylenes. Fishwick, C.W.G.; Storr, R.; Manley, P.W. *J. Chem. Soc., Chem. Commun.* 1984, 1304-1305.
97. Prostaglandins, Thromboxanes, Leukotrienes and Related Arachidonic Acid Metabolites. Lai, S.M.F.; Manley, P.W. *Nat. Prod. Rep.* 1984, *1*, 409-441.
98. Formation of 3*H*-1,3-benzodiazepines by Cycloaddition of 1,3-Oxazol-5-ones to 2-Phenylbenzazete. Manley, P.W.; Rees, C.W.; Storr, R.C. *J. Chem. Soc., Chem. Commun.* 1983, 1007-1008.
99. Synthesis of (*E*)-1-(5-Chlorothien-2-yl)-2-(1*H*-imidazol-1-yl)ethanone 2,6-dichlorophenyl-hydrazone hydrochloride, a Novel, Orally Active Antifungal Agent. *J. Med. Chem.* 1983, *26*, 442-445.
100. The Chemistry of 6-Dialkylamino-2*H*-1,3-oxazin-2-ones. Reversible Thermal Ring - Opening and Cycloaddition Reactions with *N*-Arylmaleimides and 1-diethylaminopropyne. X-Ray Crystal Structures of a 5*H*-2-Pyridone and a 1*H*-2-pyridone. *J. Chem. Soc., Perkin Trans. 1* 1981, 2878-2883.
101. Flash-Vacuum Pyrolysis of 1,3-Oxazin-6-ones and 1,2,3- and 1,2,4-Triazines: The Generation of Azetes. Glasbey, T.O.; Manley, P.W.; Storr, R.C. *J. Chem. Res., Synop.* 1981, 162-163.
102. A Simple Flash Vacuum Pyrolysis Apparatus. Campbell, J.J.A.; Halliwell, P.; Manley, P.W. *Chem. Ind. (London)* 1978, 842-843.
103. Benzazetes as Precursors for Benzotriazepines. Manley, P.W.; Somanathan, R.; Reeves, D.L.R.; Storr, R.C. *J. Chem. Soc., Chem. Commun.* 1978, 396-397.

Patents

1. Manley, Paul W.; Schoepfer, Joseph. Organic compounds. WO2008125691.
2. Chianelli, Donatella; Li, Xiaolin; Liu, Xiaodong; Loren, Jon; Molteni, Valentina; Nabakka, Juliet; Revesz, Laszlo; Perez, Lawrence B.; Brooks, Clinton; Wrona, Wojciech; Manley, Paul W.; Breitenstein, Werner. Compounds and compositions as protein kinase inhibitors. WO2008058037.
3. Manley, Paul W.; Martiny-Baron, Georg; Mestan, Juergen. Pyrimidylaminobenzamide compound Ephrin receptor kinase inhibitors, and their therapeutic use. WO2007137981.
4. Manley, Paul W. Use of c-src inhibitors in combination with a pyrimidylaminobenzamide compound for the treatment of leukemia. WO2007116025.
5. Manley, Paul W. Combination comprising a) a pyrimidylaminobenzamide compound, and b) a thr315Ile kinase inhibitor. WO2007116029
6. Burke, Gregory Peter; Linnartz, Ronald Richard; Manley, Paul W.; Versace, Richard William. Combinations of therapeutic agents for treating cancer. WO 2007115289.
7. Bold, Guido; Vaupel, Andrea; Pissot Soldermann, Carole; Manley, Paul W.. Heterobicyclic carboxamides as inhibitors for kinases. WO2007104538.
8. Capraro, Hans-Georg; Coupez, Bernard; Furet, Pascal; Manley, Paul W.; Pissot Soldermann, Carole. Sulphonamidoaniline derivatives being janus kinases inhibitors. WO2007071393.
9. Manley, Paul W. Pyrimidylaminobenzamide derivatives for the treatment of neurofibromatosis. WO2007065898.

10. Manley, Paul W.; Jacob, Sandra. Pharmaceutical combination combinations containing pyrimidylaminobenzamide and thiazolecarboxamide derivatives. WO2007051862.
11. Manley, Paul W. Pharmaceutical combination of a pyrimidylaminobenzamide and farnesyltransferase inhibitor. WO2007042465.
12. Atadja, PW; Bhalla, KN; Manley, PW. Pyrimidylaminobenzamide derivatives as antitumor agents. WO2007022044.
13. Manley, Paul W.; Bhalla, Kapil N. Antitumor agents comprising a pyrimidylamino-benzamide compound and an heat shock protein 90 inhibitor. WO2007022042.
14. Manley, PW; Shieh, W-C; Sutton, PA; Karpinski, PH.; Wu, R; Monnier, S; Brozio, J. Salts of 4-methyl-n-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide. WO2007015871.
15. Manley, PW; Shieh, W-C; Sutton, PA; Karpinski, PH; Wu, R; Monnier, S; Brozio, J. Crystalline forms of 4-methyl-n-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide. WO2007015870.
16. Manley, PW; Roesel, J. Organic compounds. WO2007010013.
17. Manley, PW; Lane, H. Combination of organic compounds. WO2007010012.
18. Alland, L; Manley, PW; Mestan, J. Combination of pyrimidylaminobenzamide compounds and imatinib for treating or preventing proliferative diseases. WO2006132930.
19. Alland, Leila; Fabbro, Doriano; Mestan, Juergen; Manley, Paul W. Use of pyrimidylamimo-benzamide derivatives for the treatment of systematic mastocytosis. WO 2006119154.
20. Manley, PW; Mestan, J; Fabbro, D. Pyrimidylaminobenzamide derivatives for hypereosinophilic syndrome. WO 2006117185.
21. Manley, PW. Pharmaceutical combination of bcr-abl and raf inhibitors. WO 2006089781
22. Manley, PW; Martiny-Baron, G; Mestan, J. Use of pyrimidylaminobenzamides for the treatment of diseases that respond to modulation of tie-2 kinase activity. WO 2006079539
23. Bold, Guido; Capraro, Hans-Georg; Caravatti, Giorgio; Floersheimer, Andreas; Furet, Pascal; Manley, Paul W.; Vaupel, Andrea; Pissot Soldermann, Carole; Gessier, Francois; Schnell, Christian; Littlewood-Evans, Amanda Jane; Kapa, Prasad Koteswara; Bajwa, Joginder S.; Jiang, Xinglong. Bicyclic amides as kinase inhibitors. WO 2006059234.
24. Cooke, Nigel Graham; Manley, Paul W. Combinations of Jak inhibitors. WO 2006056399.
25. Bold, Guido; Caravatti, Giorgio; Floersheimer, Andreas; Furet, Pascal; Manley, Paul W.; Pissot Soldermann, Carole; Vaupel, Andrea. Preparation of cyclic diaryl ureas suitable as tyrosine kinase inhibitors. WO 2006034833.
26. Fendrich, Gabriele; Jacob, Sandra Wendy; Klon, Anthony Edward; Manley, Paul William. Three-dimensional structure of c-Abl. US 2006030017.
27. Ding, Qiang; Gray, Nathanael Schiander; Li, Bing; Liu, Yi; Sim, Taebo; Uno, Tetsuo; Zhang, Guobao; Pissot Soldermann, Carole; Breitenstein, Werner; Bold, Guido; Caravatti, Giorgio; Furet, Pascal; Guagnano, Vito; Lang, Marc; Manley, Paul W.; Schoepfer, Joseph; Spanka, Carsten. Pyrimidine urea derivatives as kinase inhibitors. WO 2006000420.
28. Buerger, Hans Michael; Manley, Paul William; Mutz, Michael. Salt forms of 4-(4-methylpiperazin-1-ylmethyl)-n-[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]-benzamide. WO 2005075454.
29. Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry Min-Jian; Kinder, Frederick Ray; Lane, Heidi; Latour, Elisabeth Jeanne; Manley, Paul William; Wood, Jeanette Marjorie. Combinations of a VEGF receptor inhibitor with other therapeutic agents. WO 2005027972/3.
30. Bold, Guido; Furet, Pascal; Manley, Paul William. Anthranilic acid amide derivatives and their pharmaceutical use. WO 2004052884.

31. Manley, Paul William; Breitenstein, Werner; Jacob, Sandra; Furet, Pascal. Novel pyrimidineamide derivatives and the use thereof. WO 2004/029038.
32. Breitenstein, Werner; Furet, Pascal; Jacob, Sandra; Manley, Paul William. Inhibitors of tyrosine kinases. WO 2004/005281.
33. Floersheimer, Andreas; Furet, Pascal; Manley, Paul William; Bold, Guido; Boss, Eugen; Guagnano, Vito; Vaupel, Andrea. Preparation of diaryhurea derivatives useful for the treatment of protein kinase dependent diseases. WO 2003/099771.
34. Bold, Guido; Furet, Pascal; Manley, Paul William. Anthranilic acid amides and their use as VEGF receptor tyrosine kinase inhibitors. WO 2003/40102.
35. Bold, Guido; Furet, Pascal; Manley, Paul William. Preparation of pyridyl-substituted anthranilic acid amides for treating neoplastic disease. WO 200340101.
36. Griffin, James Douglas; Manley, Paul William. Staurosporine derivatives as inhibitors of FLT3 receptor tyrosine kinase activity. WO 2003/37347.
37. Donato, Nicholas J.; Fabbro, Doriano; Manley, Paul William; Mestan, Juergen; Warmuth, Markus; Hallek, Michael; Talpaz, Moshe; Wu, Ji. Use of c-Src inhibitors alone or in combination with STI571 for the treatment of leukaemia. WO 2003/13540.
38. Bold, Guido; Manley, Paul William; Martin-Kohler, Andreas; Sequin, Urs. Oxazolo-and furopyrimidines and their use in medicaments against tumors. WO 2002/092603.
39. Capraro, Hans-Georg; Furet, Pascal; Garcia-Echeverria, Carlos; Manley, Paul William. 4-amino-5-phenyl-7-cyclobutyl-pyrrolo (2,3-d) pyrimidine derivatives. WO 2002/092599.
40. Bold, Guido; Manley, Paul William. Phthalazine derivatives with angiogenesis inhibiting activity. WO 2002/090346.
41. Buerger, Hans Michael; Caravatti, Giorgio; Zimmermann, Juerg; Manley, Paul William; Breitenstein, Werner; Cudd, Margaret Amelia. N-phenyl-2-pyrimidinamine derivatives as tyrosine kinase inhibitors. WO 2002/022597.
42. Pyridine derivatives inhibiting angiogenesis and/or VEGF receptor tyrosine kinase. Bold, Guido; Manley, Paul William. WO 2001/58899.
43. 2-Amino-nicotinamide derivatives and their use as VEGF-receptor tyrosine kinase inhibitors. Manley, Paul William; Bold, Guido. WO 2001/55114.
44. Phthalazine derivatives for treating inflammatory diseases. Bold, Guido; Dawson, King Janet; Frei, Jorg; Heng, Richard; Manley, Paul William; Wietfeld, Bernhard; Wood, Jeanette Marjorie. Phthalazine derivatives for treating inflammatory diseases. WO 2000/59509.
45. Anthranilic acid amides and the use thereof as medicaments. Altmann, Karl-Heinz; Bold, Guido; Furet, Pascal; Manley, Paul William; Wood, Jeanette Marjorie; Ferrari, Stefano; Hofmann, Francesco; Mestan, Jurgen; Huth, Andreas; Kruger, Martin; Seidelmann, Dieter; Menrad, Andreas; Haberey, Martin; Thierauch, Karl-Heinz. WO Pat. 2000/27820 (Novartis).
46. Anthranilic acid amides and the use thereof as medicaments. Huth, Andreas; Seidelmann, Dieter; Thierauch, Karl-Heinz; Bold, Guido; Manley, Paul William; Furet, Pascal; Wood, Jeanette Marjorie; Mestan, Jurgen; Bruggen, Jose; Ferrari, Stefano; Kruger, Martin; Ottow, Eckhard; Menrad, Andreas; Schirner, Michael. WO Pat. 2000/27819 (Novartis/Schering).
47. Isoquinoline derivatives with angiogenesis inhibiting activity. Altmann, K.-H.; Bold, G.; Manley, P. W. WO Pat. 2000/09495 (Novartis).
48. Benzopyrans having potassium channel opening activity. Manley, P.W.; Dannecker, R. WO Pat. 2000/21957 (Novartis).
49. Preparation of triaryl compounds as inhibitors of TNF-a release, PDE 4 isoenzyme activity, as immunosuppressants, and as antiinflammatories. Manley, Paul William. WO Pat. 9732853 (Novartis).
50. Benzopyrans and Pharmaceutical Compositions Containing them. Manley, P.W. WO Pat.

96/37490 (Sandoz).

51. 2,2-Dialkyl- and 2,2-Dialkyl-3,4-dihydro-3-hydroxy-2*H*-1-benzopyrans, Their Use as Pharmaceuticals. Manley, P.W. WO Pat. 94/12493 (Sandoz).
52. Preparation of 1-(2-Alkenyl)imidazoles as Thromboxane Synthetase Inhibitors. Manley, P.W.; Porter, R.A.; Lai, M.F. U.S. Pat. 4 837 333 (G.D. Searle).
53. Preparation of □-(Phenylalkyl)pyridinealkanols as Platelet Inhibitors. Manley, P.W.; Porter, R.A.; Lai, M.F. EP Pat. 267 439 (G.D. Searle).
54. □-({Phenylmethoxy)methyl}pyridinealkanol Derivatives, Procedure for their Preparation, Pharmaceutical Composition containing them and their use. Manley, P.W.; Porter, R.A.; Lai, M.F. EP Pat. 264 114 (G.D. Searle).
55. Preparation and Testing of Imidazopyridines as Platelet Activating Factor (PAF) Antagonists. Manley, P.W.; Porter, R.A. EP Pat. 260 613 (G.D. Searle).
56. Preparation of 6-(Imidazolylphenyl)-4-phenyl(imino)pyrimidinones, Useful as Hypotensive Agents. U.S. Pat. 4 708 958 (G.D. Searle).
57. (1*H*-Imidazol-1-yl)alkanoic Acid Derivatives having Anti-Thrombotic Activity. Manley, P.W.; Lai, M.F. U.S. Pat. 4 579 862 (G.D. Searle).
58. Substituted Alkenylimidazoles. Manley, P.W.; Porter, R.A.; Lai, M.F. EP Pat. 150 892 (G.D. Searle).
59. 1-(1*H*-Imidazolyl), 1-*N*-Morpholinyl and Pyridyl Compounds and their Pharmaceutical Compositions. Manley, P.W.; Lai, M.F. EP Pat. 105 575 (G.D. Searle).
60. Imidazole Hydrazone and hydrazine Derivatives. Fellner, P.J.; Ellames, G.; Floyd, C.D.; Manley, P.W. U.S. Pat. 4 377 697 (G.D. Searle).
61. Imidazole Hydrazone and hydrazine Derivatives and their use in Medicine. Ellames, G.; Floyd, C.D.; Manley, P.W.; Fellner, P.J. EP Pat. 57 461 (G.D. Searle).
62. Imidazole Hydrazones with Antibacterial Activity. Fellner, P.J.; Hamill, B.J.; Manley, P.W. Fr Demande 2 474 495 (G.D. Searle).

Presentations at Scientific Conferences

1. Design of BCR-Abl kinase inhibitors to treat imatinib-resistant leukaemia. International Symposium on Advances in Synthetic & Medicinal Chemistry Kiev, August 23-27, 2009.
2. Differences in the kinase binding modes of imatinib, nilotinib and dasatinib are reflected in Abl transphosphorylation assays. 6th International Conference: Inhibitors of Protein Kinases, Warsaw, 27 June – 1 July, 2009. ***Chairperson.***
3. Nilotinib: A step forward. 49TH Annual Scientific Meeting: British Society of Haematology, Brighton, 27 April, 2009.
4. Structure-based design & clinical efficacy of targeted anti-leukemic drugs: Imatinib, nilotinib & inhibitors of T315I mutant forms of Bcr-Abl. MEDI Lunch&Learn: Salt Lake City, ACS Meeting, 24 Mar 2009.
5. Structure-based design of nilotinib: A new therapy for resistant chronic myelogenous leukaemia (CML). 6th International Symposium for Chinese Medicinal Chemists (ISCMC). Shanghai, 28 July-1 August, 2008.
6. Nilotinib: From bench to bedside with a new therapy for chronic myelogenous leukaemia (CML). Meeting: Cellular Signaling & Molecular Medicine. Dubrovnik, Croatia, 29 May 2008.
7. The Future Perspective of Molecular Targeted Therapy based on the Experience of Imatinib Development. International Symposium on GIST Treatment. Osaka, 19 April 2008.
8. Cullinane C, Natoli A, Hui Y, Conus N, Brüggen J, Manley PW, McArthur GA. Characterization of nilotinib activity against a model of KIT-induced neoplasia using FDG-PET. Proc. Am. Assoc. Cancer Res. 49 (2008) 561, Abst. 2379.
9. Zielgerichtete Therapie der CML: Neue Option für die 2nd Line. Development of Nilotinib. Heidelberg; 1 February 2008.
10. Further TKIs for Haematological Malignancies. Second Global CML Workshop; Puerto Rico, 13 December, 2007.
11. Tasigna® (nilotinib): Discovery & profile of a new targeted BCR-ABL kinase inhibitor for CML. Targets & Targeted Drugs in CML: On the way to develop curative therapies, Vienna; 26-28 October, 2007.
12. Leukaemia Therapy: The discovery of imatinib & nilotinib. Swedish Läkemedelskongressen; Stockholm; 24 October, 2007.
13. Drug Discovery & Development for Treatment of Cancer: Tyrosine kinase inhibitors. Medical Oncology Group of Australasia 28th Annual Scientific Meeting; Melbourne, 3 August, 2007.
14. Discovery and development of the highly potent BCR-ABL specific TKI, Tasigna. Tasigna launch meeting; Berne; 14 June, 2007. ***Discussant on panel.***
15. Targeting BCR-ABL without the need for Multi-Targeted Kinase Inhibitors. 6th Annual Protein Kinase Congress; Lisbon; 22 May, 2007. ***Chairperson.***
16. Discovery of & Structural Biology Studies with Nilotinib, a Selective BCR-ABL Inhibitor for CML. Joint German-Swiss Medicinal Chemistry Meeting: "Frontiers in Medicinal Chemistry"; Berlin; 20 March, 2007
17. GNF2: A prototype allosteric inhibitor of ABL kinase. CML Workshop – Looking

Toward the Future; Bermuda; 15-16 Dec, 2006.

18. Bcr-Abl Binding Modes of Dasatinib, Imatinib and Nilotinib: An NMR Study. ASH, Orlando, FL, Dec. 9-12, 2006; #747: *Blood* 2006, 108(11 pt.1):224a.
19. Nilotinib: A new BCR-ABL inhibitor for the treatment of imatinib-resistant CML and GIST. "Targeting the Kinome" meeting, Basel, Switzerland, Dec 4-6, 2006.
20. Nilotinib: A new agent for the treatment of imatinib-resistant Chronic Myelogenous Leukaemia. Swiss Chemical Society, "*Herbstversammlung*", Zurich, 13 October 2006.
21. New kinase inhibitors for the treatment of hematological malignancies and gastrointestinal stromal tumors. 232nd ACS National Meeting, San Francisco, CA, United States, Sept. 10-14, 2006; #MEDI-319.
22. Nilotinib: A Novel Bcr-Abl Kinase Inhibitor for the Treatment of Chronic Myelogenous Leukemia. Asia Pacific Education Center of Hematology / Oncology, Shanghai, 29 Aug, 2006.
23. Case Study: Gleevec - A New Treatment Modality for CML, Drug Discovery Technologies Europe, London, March 14-14, 2006.
24. Targeted Anti-Cancer Drugs: Not just for the treatment of CML. 8th China-Novartis Symposium, Cancer, Hanghzou, China. Nov 1-3, 2005.
25. Medicinal chemistry versus Bcr-Abl. Gordon Research Conference: Medicinal Chemistry, New London, NH; August 2005.
26. Advances in the Structural Biology, Design and Clinical Development of Bcr-Abl Kinase Inhibitors for the Treatment of Chronic Myelogenous Leukemia. 4th International Conference on Inhibitors of Protein Kinases. Warsaw; June 2005.
27. AMN107: A Novel Bcr-Abl Kinase Inhibitor for the Treatment of Chronic Myelogenous Leukemia. Pharm. Sci. Fair: Anti-Cancer Agents. Nice; June, 2005.
28. Case History: Imatinib. Cambridge, MA; June 2005. ***Faculty.***
29. Design and Synthesis of PDE472. Organic Synthesis and Process Chemistry. Hyderabad, 1-3 April, 2005
30. Structural biology guided optimization of tyrosine kinase inhibitors: AMN107 a selective and potent Bcr-Abl inhibitor. 229th ACS National Meeting, San Diego, CA, United States, March 13-17, 2005, MEDI-309. ***Chairperson/Session Organiser.***
31. Glivec: A case history. Swiss Course on Medicinal Chemistry. Leysin, Switzerland. October, 2004. ***Faculty.***
32. AMN107. Novartis Course on Medicinal Chemistry. Boston, MS. October, 2004. ***Faculty.***
33. Anthranilic Acid Derivatives: VEGF-R Kinase Inhibitors for Anti-angiogenic Therapy in Cancer. 18th International Symposium on Medicinal Chemistry, Copenhagen, August 2004.
34. Targeted drugs for cancer therapy: Glivec a new paradigm. 15th International Symposium on Molecular Biology of Haematopoiesis. Tokyo, August 2004.
35. Targeted drugs for cancer therapy. Gleevec: a new paradigm. Gesellschaft Deutscher Chemiker Aachen, June, 2004.
36. Targeted drugs for cancer therapy. Gleevec: a new paradigm. Freiburger Chemischen Gesellschaft, Feb., 2004.
37. Targeted drugs for cancer therapy. Gleevec: a new paradigm. New therapies for the treatment of cancer. North Eastern ACS Meeting, Cambridge, MS; December 2003.
38. A novel anthranilamide, as an anti-angiogenic VEGF receptor kinase inhibitor. Autumn Meeting of Swiss Chemical Society, Lausanne, 2003.

39. Glivec: A case history. 23RD Advanced Course on Medicinal Chemistry. Urbino, Italy. July, 2003. **Faculty.**
40. Advances with VEGF-R Kinase Inhibitors for the Treatment of Angiogenesis. 3rd International Conference on Inhibitors of Protein Kinases . Warsaw, June 2003. ***Chairperson.***
41. Targeted drugs for cancer therapy: A new paradigm. *CHEM 267.* Berkeley, CA. April, 2003.
42. STI571 (imatinib): A targeted drug for cancer. Biozentrum, Basel, January 2003.
43. PKC412 (Midostaurin): an Flt3 inhibitor with potential for the therapy of acute myelogenous leukemia. "Protein Phosphorylation". San Diego, March, 2003. *CHAIRPERSON.*
44. Targeted Cancer Medicine - a look into the future. European School of Oncology Winter-Masterclass: Clinical Oncology. Tenerife, 24 January, 2003.
45. Structural and enzymatic studies of interactions with Abl kinase and resistance mutants. "Protein Kinases in Drug Discovery & Development". San Francisco, October, 2002. *CHAIRPERSON.*
46. Molecular therapy of cancer – glivec and beyond. Taipei. September, 2002.
47. STI571 (imatinib): An inhibitor of Bcr-Abl activation. Granta Park Symposium. Cambridge. June 2002.
48. Glivec: A case history. Swiss Course on Medicinal Chemistry. Leysin, Switzerland. October, 2002.
49. Discovery of STI571 and preclinical studies. Tieteellinen juhlasymposium, Glivec: molekyylitasolta ihmisen elämään. Helsinki; March, 2002.
50. Molecular Design of Tyrosine Kinase Inhibitors. Second International Symposium on GIST- Tyrosine Kinase Inhibitors in Treatment of Solid Tumors. Helsinki, September, 2001.
51. Structure and Molecular Design of Tyrosine Kinase Inhibitors. Second International Symposium on GIST- Tyrosine Kinase Inhibitors in Treatment of Solid Tumors. Helsinki, September, 2001.
52. GLEEVEC (STI571): A tyrosine kinase inhibitor tailored for leukemia therapy. Gordon Conference on Medicinal Chemistry, New Hampshire, August, 2001.
53. Glivec and PTK787: Tailored kinase inhibitors for fitting cancer therapy. Society of Chemical Industry conference: "Protein Kinases: Good Targets of Drug Discovery", London, May 2001.
54. PTK787 / ZK222584. Discovery and Antiangiogenic Profile of a Selective VEGFR-2 Kinase Inhibitor. Gordon Conference on Medicinal Chemistry, New Hampshire, August, 2000.
55. Potassium Channel Activators for the Treatment of Asthma. and Disease. International Conference on ATP-Sensitive Potassium Channels and Disease, Illinois, July, 1998.
56. Potassium Channel Activators for the Treatment of Asthma: 6-Pyridylbenzopyran Derivatives. 214th ACS Meeting, Las Vegas, September, 1997.
57. PDE 4 Inhibitors: Design, synthesis and antiinflammatory activity of 4-(3-cyclopentylidenemethyl-4-methoxyphenyl)pyridine. Autumn Meeting of Swiss Chemical Society, Basel, 1996.
58. Structure-Activity Studies of Potassium Channel Opening in Pinacidil-Type Cyanoguanidines and Nitroethenediamines. Autumn Meeting of Swiss Chemical Society, Bern, 1991.

Posters at Scientific Conferences

1. Pierre Laneuville, Clifford DiLea, Jürgen Mestan, Ophelia Yin, Richard C. Woodman,

Paul W. Manley. Comparative In Vitro Cellular Data Alone is Insufficient To Predict Clinical Responses and Guide Choice of BCR-ABL Inhibitor To Treat Imatinib-Resistant Chronic Myeloid Leukemia (CML). *Blood* 2009;114(11 pt.1):#.

2. David A. Irvine, Bin Zhang, Elaine C. Allen, Tessa L. Holyoake, Marion Dorsch, Paul Manley, Ravi Bhatia, Mhairi Copland. The combination of Hedgehog pathway inhibitor LDE225 and nilotinib eliminates chronic myeloid leukemia stem and progenitor cells. *Blood* 2009;114(11 pt.1):#.

3. Pierre Laneuville, Clifford DiLea, Jürgen Mestan, Ophelia Yin, Paul W. Manley. Comparitive in vitro cellular data alone is insufficient to guide choice of BCR-Abl inhibitor to treat imatinib-resistant chronic myeloid leukemia (CML). European Society Haematology, Berlin, 6 June, 2009.

4. Paul W. Manley, Sandra Cowan-Jacob, Gabriele Fendrich, Janis Liebetanz, Jürgen Mestan, Nicole Martin, Doriano Fabbro. The inhibition of ABL kinase activity by nilotinib and imatinib, but not dasatinib, is time-dependent. *Proc. Am. Assoc. Cancer Res.* 2009;50:897.

5. Cullinane C, Natoli A, Hui Y, Conus N, Brueggen J, Manley PW, McArthur GA. Characterization of nilotinib activity against a model of KIT-induced neoplasia using FDG-PET. *Proc. Am. Assoc. Cancer Res.* 2008;49:561.

6. Davies A., Giannoudis A., Lucas C.M., Harris R.J., Manley P.W., Pirmohamed M., Clark R.E. Characterisation of nilotinib transport in CML cells. *Blood* 2007;118(11 pt.1):698a.

7. Extended kinase profiling of the BCR-ABL inhibitor nilotinib. Paul W. Manley, Josef Brüggen, Doriano Fabbro, Georg Martiny-Baron, Jürgen Mestan and Thomas Meyer. *Proc. Am. Assoc. Cancer Res.* 2007;48:772.

8. AMN107: Efficacy of the selective Bcr-Abl tyrosine kinase inhibitor in a murine model of chronic myelogenous leukemia. Michael Rugaard Jensen, Josef Brüggen, Clifford DiLea, Jürgen Mestan, Paul W. Manley. *Proc. Am. Assoc. Cancer Res.* 2006, 47:61-62.

9. Results with AMN107, a novel kinase inhibitor, in gastrointestinal stromal tumor (GIST): Preclinical rationale and early results in a patient (Pt) with imatinib (IM)-resistant GIST. P. Dileo, S. Bauer, A. Van den Abbeele, J. A. Morgan, S. George, J. M. Salesi, L. Veronese, P. Manley, J. A. Fletcher, G. D. Demetri. Gastrointestinal Cancers Symposium, San Francisco, 2006.

10. *In vivo* activity of AMN107, as selective Bcr-Abl kinase inhibitor, in murine leukemia models. J. Mestan, J. Brueggen, D. Fabbro, P. W. Manley, G. Gilliland, B. Huntly, E. Weisberg and J. D. Griffin. Journal of Clinical Oncology, 2005 ASCO Annual Meeting Proceedings. Vol 23, No 16S (June 1 Supplement), 2005: 6522.

11. Molecular Interactions Between the Highly Selective pan-Bcr-Abl Inhibitor, AMN107, and the Tyrosine Kinase Domain of Abl. Paul W. Manley, Sandra W. Cowan-Jacob, Gabriele Fendrich, Jürgen Mestan. *Blood* 2005, 106(11 pt.1):940a-941a.

12. AMN107: Efficacy as a selective inhibitor of the tyrosine kinase activity of Bcr-Abl in murine leukemia models. Paul W. Manley, Josef Brüggen, Sandra Cowan-Jacob, Doriano Fabbro, Gabriele Fendrich, Gary Gilliland, Brian Huntly, Andrew Kung, Jürgen Mestan, Ellen Weisberg, James D. Griffin. Blood 2004, 103(11 pt.1): Abst#.

13. AMN107: In vitro profile of a new inhibitor of the tyrosine kinase activity of Bcr-Abl. J. Mestan, E. Weisberg, S. Cowan-Jacob, D. Fabbro, P. Furet, G. Fendrich, G. Goutte, D. Kempf, M. Gaugler, J. D. Griffin, P. W. Manley. Blood 2004, 103(11 pt.1): Abst#.

14. Jürgen Mestan, Paul Manley, Thomas Meyer, Doriano Fabbro. An ELISA for PDGFR Phosphorylation: Comparison of effects of STI571 on Bcr-Abl, c-Kit and PDGFR-β

protein kinases. *PROC AM ASSOC CANCER RES* 2004, 45:Abs#1500.

15. Jürgen Mestan, Dominique Kempf, Gerard Goutte, Jonathan Fletcher, Paul Manley. A New ELISA for Cellular c-Kit Phosphorylation: Activity of STI571 Compared to that of other Protein Kinase Inhibitors. Blood 2003, 102(11 pt.2): Abs#4387.
16. Crystal structure of unphosphorylated c-Src in complex with an analogue of GleevecTM reveals relative orientations of the SH3, SH2 and kinase domains in the active conformation. Cowan-Jacob, Sandra W.; Fendrich, Gabriele; Liebetanz, Janis; Fabbro, Doriano; Manley, Paul W. Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003.
17. Preclinical profile of PKC412 (midostaurin) as an FLT3 inhibitor for the treatment of AML. P.W. Manley, C. Boulton, G. Caravatti, J. Griffin, A. Kung, L. Kelly, M. Maira, J. Mestan, T. Meyer, S. Ruetz, E. Weisberg, D. Fabbro. *PROC AM ASSOC CANCER RES* 2003, 44:Abs 1004.
18. AAL993/ZK260255: A member of the novel anthranilic acid amide class of antiangiogenic VEGF receptor kinase inhibitors. Paul Manley, Guido Bold, Josef Brüggen, Pascal Furet, Jürgen Mestan, Thomas Meyer, Christian Schnell, Barbara Stolz, Jeanette Wood. *PROC AM ASSOC CANCER RES* 2003, 43:Abs 4697.
19. Molecular interactions between Gleevec and isoforms of the cAbl kinase. Paul Manley, Doriano Fabbro, Gabriele Fendrich, Pascal Furet, Sandra Jacob, Janice Liebetanz, Jürgen Mestan, Thomas Meyer. *PROC AM ASSOC CANCER RES* 2002, 43:Abs 4196. ***Selected for oral presentation.***
20. NVP-AAD777 / ZK202664, a selective VEGF receptor kinase inhibitor, which inhibits both VEGF- and bFGF-induced angiogenesis. *PROC AM ASSOC CANCER RES* 2001, 41:Abs 4470.
21. Structure-activity studies supporting a postulated binding mode of STI571 to Abl kinase. Abstr. Pap. - Am. Chem. Soc. (2001), 221st MEDI-143.
22. SAR Studies on the Angiogenesis inhibitor, PTK787 / ZK222584. 27th National Medicinal Chemistry Symposium, Kansas, June, 2000.
23. Rationalisation of the selective inhibition of VEGFR-tyrosine kinases by the angiogenesis inhibitor PTK 787 / ZK222584, on the basis of shape complementarity to hydrophobic domains within the ATP-binding site. AACR-NCI-EORTC Meeting on "Molecular Targets and Cancer Therapeutics", Washington, DC, November, 1999.
24. PDE 4 Inhibitors: Design, synthesis and antiinflammatory activity of 4-(3-cyclopentylidine-methyl-4-methoxyphenyl)pyridine. 212th ACS Meeting, San Diego, April, 1996.